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<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR</i>			
<input type="checkbox"/>	L1	moraxell\$.ti,ab,clm.	777
<input type="checkbox"/>	L2	toxin or cytotoxin or cytolysin or cyto-toxin or cyto-lysin or cytolytic or cyto-lytic or corneotoxin or corneo-toxin or corneotoxic or hemolytic or hemolysis or hemo-lytic or hemolysin or hemo-lysin	77159
<input type="checkbox"/>	L3	L2 and l1	160
<input type="checkbox"/>	L4	L2ti,ab,clm. and l1	0
<input type="checkbox"/>	L5	L2.ti,ab,clm. and l1	63
<input type="checkbox"/>	L6	(george.in. or angelos!.in. or hess.in.) and l1	10
<input type="checkbox"/>	L7	l6 and tifton\$	1

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51. [WO 200257281A](#). New aminoglycoside compounds used for treating bacterial infections caused by bacterium including Escherichia coli, Pseudomonas spp., Proteus spp., Bacteroids spp. and Haemophilus influenzae. HADDAD, J, et al. A61K031/704 C07H000/00 C07H015/224.

52. [US20020115621A](#). New macrolide compound useful as antibacterial and antiprotozoal agent for mammals. CHEN, Y, et al. A61K031/70 A61K031/7048 A61K031/7052 A61P031/04 A61P033/02 A61P043/00 C07H017/08.

53. [WO 200192280A](#). New hygromycin derivatives used for treating bacterial and protozoal infections e.g. pneumonia, otitis media, sinusitis or bronchitis. HAYWARD, M M, et al. A61K031/341 A61K031/357 A61K031/36 A61K031/443 A61K031/496 A61K031/655 A61K031/70 A61K031/7004 A61K031/7034 A61K031/7048 A61P031/04 A61P031/10 A61P033/02 C07D317/66 C07D405/02 C07D405/14 C07D407/12 C07H000/00 C07H015/203.

54. [WO 200116172A](#). Novel *Moraxella bovis* antigen useful in compositions for raising immune response in an animal, has protease, lipase or hemolysin activity. FAM, J, et al. A61K038/48 A61K039/095 C07K014/22 C07K016/12 C12N015/31.

55. [US20020061281A](#). Aerosol composition for treatment of sinusitis comprising one or more anti-infective, anti-inflammatory and/or anti-mucolytic agents e.g. cefuroxime. HALE, M A, et al. A61K009/00 A61K009/12 A61K009/14 A61K047/02 A61K047/34 A61L000/00 A61L009/04 A61P011/02 A61P031/00.

56. [WO 200064457A](#). Composition having genetically modified live oral commensal bacteria which express immunogenic fragments of mucosal pathogens, used as oral vaccines to treat host against *Bordetella pertussis*, poliovirus infection. HALPERIN, S A, et al. A61K035/00 A61K039/00 A61K048/00 C12N001/20.

57. [WO 200034297A](#). New carbamate and carbazate ketolide derivatives, useful for treatment of bacterial and protozoal infections and related disorders e.g. pneumonia, otitis media, bronchitis, rheumatic fever, glomerulonephritis and ulcers. KANEKO, T, et al. A61K031/70 A61P031/04 A61P033/02 C07D421/00 C07H017/08.

58. [US 6365574B](#). Non-hygroscopic azithromycin ethanolate compounds useful for treating microbial infections and a method for their preparation. ARONHIME, J, et al. A01N043/04 A61K000/00 A61K031/70 A61K031/7048 A61K031/7052 A61P031/04 C07H001/00 C07H017/00 C07H017/02 C07H017/08.

59. [US20020040007A](#). New macrolide derivatives, useful for treatment of e.g. bacterial and protozoal infections and related disorders e.g. pneumonia and rheumatic fever, and cancer. KANEKO, T, et al. A61K000/00 A61K031/70 A61K031/7048 A61P001/00 A61P001/02 A61P001/04 A61P009/00 A61P009/10 A61P011/00 A61P011/14 A61P013/02 A61P013/12 A61P015/00 A61P027/02 A61P027/16 A61P031/04 A61P033/00 A61P033/02 A61P035/00 C07H017/00 C07H017/08.

60. [WO 200018434A](#). New mutant cholera holotoxin having a point mutation at amino acid position 29 of the A subunit useful as an adjuvant in an antigenic composition to enhance the immune

response in a vertebrate host to a selected antigen from a pathogen. ELDRIDGE, J H, et al. A61K039/00 A61K039/002 A61K039/02 A61K039/095 A61K039/102 A61K039/106 A61K039/12 A61K039/15 A61K039/155 A61K039/245 A61K039/39 A61P037/04 C07K014/14 C07K014/22 C07K014/28 C07K014/285 C07K014:28 C12N001/15 C12N001/19 C12N001/21 C12N005/10 C12N015/09 C12N015/63 C12P021/02.

- 61. US 6342497B. New 2"-deoxy-hygromycin A derivatives used for treating bacterial and protozoal infections. LINDE, R G. A61K031/36 A61K031/4409 A61K031/70 A61K031/7048 A61P031/04 C07D000/00 C07D317/46 C07D405/10 C07D405/14 C07H015/26.
- 62. US 6313100B. New hygromycin A derivatives used for treating bacterial and protozoal infections. BRIGHTY, K E, et al. A61K031/70 A61K031/7048 A61K039/02 A61P031/00 A61P031/04 A61P033/02 C07D000/00 C07H015/00 C07H015/203 C07H015/26 C12P001/04 C12P019/00 C12P019/44 C12P019/46 C12P019/54.
- 63. WO 9007525A. Keratoconjunctivitis cytotoxin from Moraxella bovis - toxic to bovine peripheral blood neutrophils but lacks haemolytic activity. GEORGE, L W, et al. A61K037/48 A61K039/02 C07K015/00.

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Term	Documents
(1 AND (2.TI,AB,CLM.)).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	63
(L2.TI,AB,CLM. AND L1).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	63

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51. WO 200257281A. New aminoglycoside compounds used for treating bacterial infections caused by bacterium including Escherichia coli, Pseudomonas spp., Proteus spp., Bacteroids spp. and Haemophilus influenzae. HADDAD, J, et al. A61K031/704 C07H000/00 C07H015/224.

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53. WO 200192280A. New hygromycin derivatives used for treating bacterial and protozoal infections e.g. pneumonia, otitis media, sinusitis or bronchitis. HAYWARD, M M, et al. A61K031/341 A61K031/357 A61K031/36 A61K031/443 A61K031/496 A61K031/655 A61K031/70 A61K031/7004 A61K031/7034 A61K031/7048 A61P031/04 A61P031/10 A61P033/02 C07D317/66 C07D405/02 C07D405/14 C07D407/12 C07H000/00 C07H015/203.

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59. US20020040007A. New macrolide derivatives, useful for treatment of e.g. bacterial and protozoal infections and related disorders e.g. pneumonia and rheumatic fever, and cancer. KANEKO, T, et al. A61K000/00 A61K031/70 A61K031/7048 A61P001/00 A61P001/02 A61P001/04 A61P009/00 A61P009/10 A61P011/00 A61P011/14 A61P013/02 A61P013/12 A61P015/00 A61P027/02 A61P027/16 A61P031/04 A61P033/00 A61P033/02 A61P035/00 C07H017/00 C07H017/08.

60. WO 200018434A. New mutant cholera holotoxin having a point mutation at amino acid position 29 of the A subunit useful as an adjuvant in an antigenic composition to enhance the immune

response in a vertebrate host to a selected antigen from a pathogen. ELDRIDGE, J H, et al. A61K039/00 A61K039/002 A61K039/02 A61K039/095 A61K039/102 A61K039/106 A61K039/12 A61K039/15 A61K039/155 A61K039/245 A61K039/39 A61P037/04 C07K014/14 C07K014/22 C07K014/28 C07K014/285 C07K014:28 C12N001/15 C12N001/19 C12N001/21 C12N005/10 C12N015/09 C12N015/63 C12P021/02.

- 61. US 6342497B. New 2"-deoxy-hygromycin A derivatives used for treating bacterial and protozoal infections. LINDE, R G. A61K031/36 A61K031/4409 A61K031/70 A61K031/7048 A61P031/04 C07D000/00 C07D317/46 C07D405/10 C07D405/14 C07H015/26.
- 62. US 6313100B. New hygromycin A derivatives used for treating bacterial and protozoal infections. BRIGHTY, K E, et al. A61K031/70 A61K031/7048 A61K039/02 A61P031/00 A61P031/04 A61P033/02 C07D000/00 C07H015/00 C07H015/203 C07H015/26 C12P001/04 C12P019/00 C12P019/44 C12P019/46 C12P019/54.
- 63. WO 9007525A. Keratoconjunctivitis cytotoxin from Moraxella bovis - toxic to bovine peripheral blood neutrophils but lacks haemolytic activity. GEORGE, L W, et al. A61K037/48 A61K039/02 C07K015/00.

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Term	Documents
(1 AND (2.TI,AB,CLM.)).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	63
(L2.TI,AB,CLM. AND L1).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	63

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- tr Q43892 _ACTAC Leukotoxin [LKTA] [Actinobacillus actinomycetemc
- tr Q46716 _ECO57 Hemolysin A (Hemolysin toxin protein) [hlyA] [Es
- tr P71223 _ECOLI EHEC-hemolysin [EHEC-hlyA] [Escherichia coli]
- sp P55129 RTX12_ACTPL RTX-I toxin determinant A from serotypes 5.
- sp P55128 RTX11_ACTPL RTX-I toxin determinant A from serotypes 1.
- tr Q47461 _ECOLI EHEC-hlyA protein [EHEC-hlyA] [Escherichia coli]
- tr Q47262 _ECOLI Hemolysin [EHEC-hlyA] [Escherichia coli]
- sp P16462 LKTA_ACTAC Leukotoxin (Lkt) [lktA] [Actinobacillus act.
- tr Q79D75 _ECOLI HlyA (Fragment) [hlyA] [Escherichia coli]
- tr Q5MK37 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae]
- tr Q5MK35 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae]
- tr Q5MK32 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae]
- tr Q5MK34 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae]
- tr Q5MK29 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae]
- tr Q5MK27 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae]
- tr Q5MK36 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae]
- tr Q5MK40 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae]
- tr Q5MK38 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae]
- tr Q5MK39 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae]
- tr Q5MK41 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae]
- tr Q5MK33 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae]
- tr Q5MK26 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae]
- tr Q5MK28 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae]
- tr Q5MK30 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae]
- tr Q5MK25 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae]
- sp Q57506 CYAA_BORBR Bifunctional hemolysin-adenylate cyclase pr.
- sp P15318 CYAA_BORPE Bifunctional hemolysin-adenylate cyclase pr.
- tr Q7W1N2 _BORPA Bifunctional hemolysin-adenylate cyclase (EC 4.6
- tr Q9L469 _BORPA Bifunctional hemolysin-adenylate cyclase (EC 4.6
- tr Q3SAJ8 _9BORD Adenylate cyclase toxin [cyaA] [Bordetella hinzi]
- tr Q2PUJ2 _MANGL Leukotoxin structural protein (Fragment) [lktA]
- tr Q2PUJ8 _PASHA Leukotoxin structural protein (Fragment) [lktA]
- tr Q2PUJ6 _MANGL Leukotoxin structural protein (Fragment) [lktA]
- tr Q2PUH9 _9PAST Leukotoxin structural protein (Fragment) [lktA]
- tr Q2PUI3 _9PAST Leukotoxin structural protein (Fragment) [lktA]
- tr Q2PUI7 _PASHA Leukotoxin structural protein (Fragment) [lktA]
- tr Q2PUI8 _MANGL Leukotoxin structural protein (Fragment) [lktA]
- tr Q2PUI5 _9PAST Leukotoxin structural protein (Fragment) [lktA]
- tr Q5MK31 _9PAST Leukotoxin A (Fragment) [lktA] [Pasteurellaceae]
- tr Q2PUI7 _9PAST Leukotoxin structural protein (Fragment) [lktA]
- tr Q2PUI6 _9PAST Leukotoxin structural protein (Fragment) [lktA]
- tr Q2PUH6 _9PAST Leukotoxin structural protein (Fragment) [lktA]

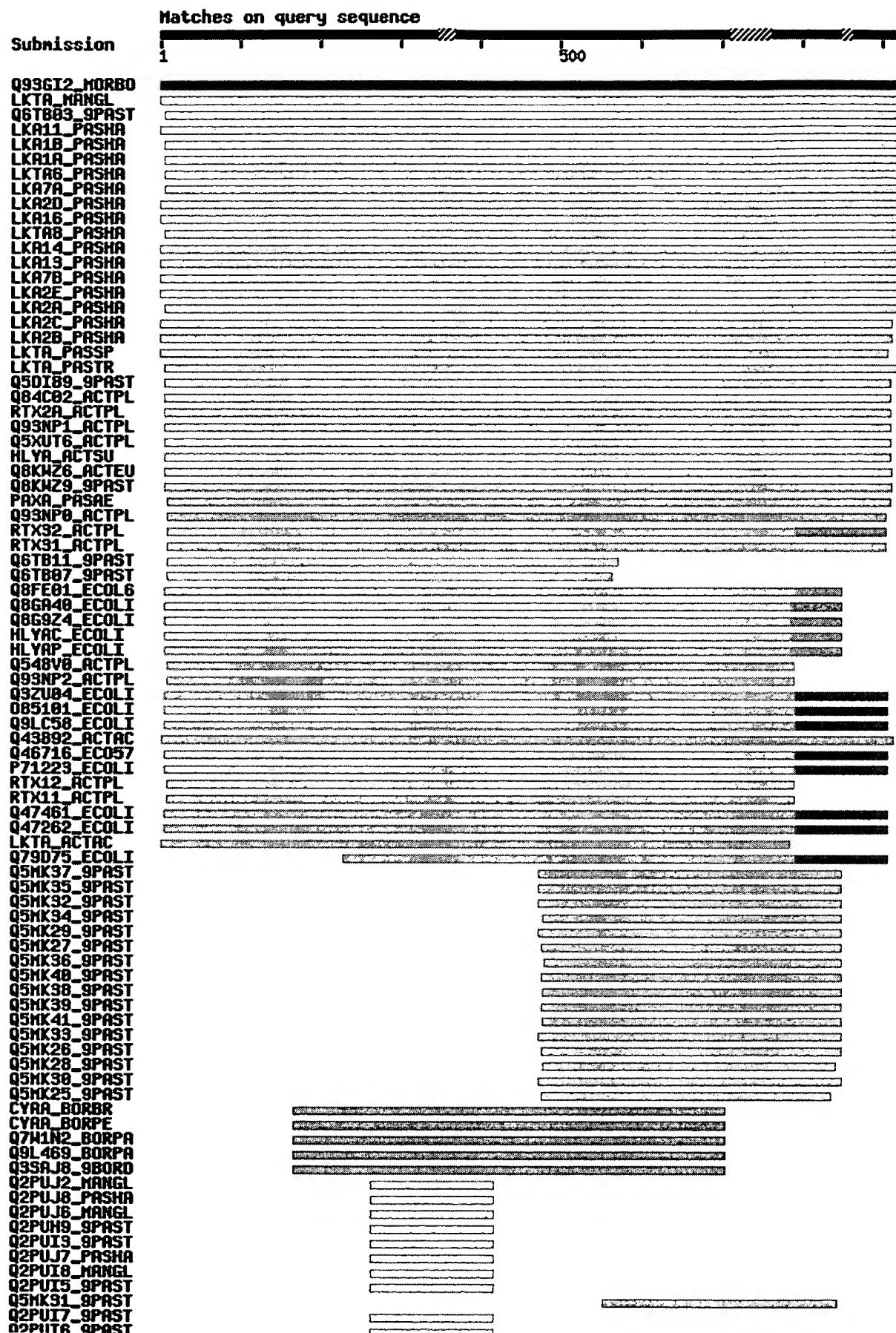
- tr Q2PUH5 _9PAST Leukotoxin structural protein (Fragment) [lktA]
- tr Q2PUI1 _9PAST Leukotoxin structural protein (Fragment) [lktA]
- tr Q6RKA4 _ECOLI HlyA (Fragment) [Escherichia coli]
- tr O68404 _ECOLI Alpha hemolysin (Fragment) [hylA] [Escherichia c
- tr O70070 _ECOLI Alpha hemolysin (Fragment) [hylA] [Escherichia c
- tr O68403 _ECOLI Alpha hemolysin (Fragment) [hylA] [Escherichia c
- tr Q8VQ26 _ECOLI HlyA (Fragment) [Escherichia coli]
- tr Q8VQ38 _9ENTR HlyA (Fragment) [hlyA] [Citrobacter rodentium]
- tr Q83WM0 _ECO57 Hemolysin (Fragment) [hlyA] [Escherichia coli O1
- tr Q937W0 _BORBR Adenylate cyclase hemolysin (Fragment) [cyaA] [B
- tr Q937V6 _BORBR Adenylate cyclase hemolysin (Fragment) [cyaA] [B
- tr Q937W1 _BORBR Adenylate cyclase hemolysin (Fragment) [cyaA] [B
- tr Q937V9 _BORBR Adenylate cyclase hemolysin (Fragment) [cyaA] [B
- tr Q937V8 _BORBR Adenylate cyclase hemolysin (Fragment) [cyaA] [B

Graphical overview of the alignments

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Alignments

tr Q93GI2 RTX toxin [mbxA] [Moraxella bovis] 92
 Q93GI2_MORBO al:

Score = 1612 bits (4175), Expect = 0.0
 Identities = 850/927 (91%), Positives = 850/927 (91%)

Query: 1 MSNINVIKSNIQAGLNSTKGLKNLYLAIPKDYDPQKGGLNDFIKAADELGIARL
 MSNINVIKSNIQAGLNSTKGLKNLYLAIPKDYDPQKGGLNDFIKAADELGIARL
 Sbjct: 1 MSNINVIKSNIQAGLNSTKGLKNLYLAIPKDYDPQKGGLNDFIKAADELGIARL

Query: 61 NHTETAKKSVDVNQFLSLTQTGIAISATKLEKFLQKHSTNKLAKGLDSVENIDRK
 NHTETAKKSVDVNQFLSLTQTGIAISATKLEKFLQKHSTNKLAKGLDSVENIDRK
 Sbjct: 61 NHTETAKKSVDVNQFLSLTQTGIAISATKLEKFLQKHSTNKLAKGLDSVENIDRK

Query: 121 SNVLSTLSSFLGTALAGIELDSLICKGDAAPDALAKASIDLINIEIIGNLSQSTQTI
 SNVLSTLSSFLGTALAGIELDSLICKGDAAPDALAKASIDLINIEIIGNLSQSTQTI
 Sbjct: 121 SNVLSTLSSFLGTALAGIELDSLICKGDAAPDALAKASIDLINIEIIGNLSQSTQTI

Query: 181 SQLAKLGSTISQAKGFSNIGNKLQNLNFSTNLGLEIITGLSGISAGFALADKNA
 SQLAKLGSTISQAKGFSNIGNKLQNLNFSTNLGLEIITGLSGISAGFALADKNA
 Sbjct: 181 SQLAKLGSTISQAKGFSNIGNKLQNLNFSTNLGLEIITGLSGISAGFALADKNA

Query: 241 KVAAGFELSNQVIGNVTKAISSYVLAQRVAAGLSTTGAVAALITSSIMLAISPLAF
 KVAAGFELSNQVIGNVTKAISSYVLAQRVAAGLSTTGAVAALITSSIMLAISPLAF
 Sbjct: 241 KVAAGFELSNQVIGNVTKAISSYVLAQRVAAGLSTTGAVAALITSSIMLAISPLAF

Query: 301 DKFNHANALDEFQFRKFGYDGDHLLAEYQRGVGTIEASLTTISTALXXXXXXXX
 DKFNHANALDEFQFRKFGYDGDHLLAEYQRGVGTIEASLTTISTAL
 Sbjct: 301 DKFNHANALDEFQFRKFGYDGDHLLAEYQRGVGTIEASLTTISTALGAVSAGVS

Query: 361 XXXXXXPIALLVAGVTGLISGILEASKQAMFESVANRLQGKILEWEKQNGGQNYFD
 PIALLVAGVTGLISGILEASKQAMFESVANRLQGKILEWEKQNGGQNYFD
 Sbjct: 361 GSAVGAPIALLVAGVTGLISGILEASKQAMFESVANRLQGKILEWEKQNGGQNYFD

Query: 421 SRYAAYLANNLKFLSELNKELEAERVIAITQQRWDNNIGELAGITKLGERIKSGKA
 SRYAAYLANNLKFLSELNKELEAERVIAITQQRWDNNIGELAGITKLGERIKSGKA
 Sbjct: 421 SRYAAYLANNLKFLSELNKELEAERVIAITQQRWDNNIGELAGITKLGERIKSGKA

Query: 481 FEDGKKVEAGSNITLDAKTGIIDISNSNGKKTQALHFTSPLLTAGTESRERLTNGK
 FEDGKKVEAGSNITLDAKTGIIDISNSNGKKTQALHFTSPLLTAGTESRERLTNGK
 Sbjct: 481 FEDGKKVEAGSNITLDAKTGIIDISNSNGKKTQALHFTSPLLTAGTESRERLTNGK

Query: 541 NKLKFGRVKNWQVTDGEASSKLDTSKVIQRVAETEGTDEIGLIVNAKAGNDDIFVG
 NKLKFGRVKNWQVTDGEASSKLDTSKVIQRVAETEGTDEIGLIVNAKAGNDDIFVG

Sbjct: 541 NKLKFGRVKNWQVTDGEASSKLDTSKVIQRVAETEGTDEIGLIVNAKAGNDDIFVG
Query: 601 NIDGGDGHDRVYSKDGGFGNITVDGTSATEAGSYTVNRKVARGDIYHEVVKRQET
Sbjct: 601 NIDGGDGHDRVYSKDGGFGNITVDGTSATEAGSYTVNRKVARGDIYHEVVKRQET
Query: 661 RTETIQYRDYELRKVGYGYQSTDNLKSVEEVIGSQFNDVFKGSKFNDIFHSXXXXX
RTETIQYRDYELRKVGYGYQSTDNLKSVEEVIGSQFNDVFKGSKFNDIFHS
Sbjct: 661 RTETIQYRDYELRKVGYGYQSTDNLKSVEEVIGSQFNDVFKGSKFNDIFHSGEGDD
Query: 721 XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXNDVYIFRKGDGNDTLYD
N NDVYIFRKGDGNDTLYD
Sbjct: 721 GAGDDRLFGGKGNDRLSGDEGDDLLDGGSDDVLNGGAGNDVYIFRKGDGNDTLYD
Query: 781 DKLAFADANISDIMIERTKEGIIVKRNDHSGSINI PRWYITSNLQNYQSNKTDHKI
DKLAFADANISDIMIERTKEGIIVKRNDHSGSINI PRWYITSNLQNYQSNKTDHKI
Sbjct: 781 DKLAFADANISDIMIERTKEGIIVKRNDHSGSINI PRWYITSNLQNYQSNKTDHKI
Query: 841 GKDGSYITSXXXXXXXXXXGTVITSQELKKLADENKSQKLSASDIASSLNKLVG
GKDGSYITS GTVITSQELKKLADENKSQKLSASDIASSLNKLVG
Sbjct: 841 GKDGSYITSQELKKLADENKSQKLSASDIASSLNKLVG
Query: 901 FGTANSVSSNALQPITQPTQGILAPSV 927
FGTANSVSSNALQPITQPTQGILAPSV
Sbjct: 901 FGTANSVSSNALQPITQPTQGILAPSV 927

sp Q9ETX2 Leukotoxin (Lkt) [lktA] [Mannheimia glucosida] 9
LKTA_MANGL
 Score = 783 bits (2022), Expect = 0.0
 Identities = 426/935 (45%), Positives = 589/935 (62%), Gaps = 25/9
 Query: 2 SNINVIKSNIQAGLNSTKGLKNLYLAIPKDY--DPQKGTLNDFIKADELGIAR
 S +N ++ S K+G K + L IPKDY D +KG L D +KAA+ELGI
 Sbjct: 21 SGLNRTGQSLAKAGQSLKTGAKKIIILYIPKDYQYDTEKGNGLQDLVKAEEELGIEV
 Query: 60 PNHTETAKKSVDVNQFLSLTQTGIAISATKLEKFLQKHSTNKLAKGLDSVENIDR
 N A+ S+ T+ L LT+ GI +SA +L+K LQK K+ + + S EN+ +
 Sbjct: 81 GNDIAKAQTSLGTIQNVLGLTERGIVLSAPQLDKLLQK---TKVGQAIGSAENLTK
 Query: 120 ASNVLSTLSSFLGTALAGIELDSLICKGDAAPDALAKASIDLNEIIGNLSQSTQT
 A VLS + S LG+ LAG++LD ++K ++ LAKA ++L N +I N++ S +T
 Sbjct: 138 AKTVLSGIQSILGSVLAGMDLDEALQK-NSNELTLAKAGLELTNSLIENIANSVKT
 Query: 180 SSOLAKLGSTISOAKGFSNIGNKLONLN-FSKTNLGLEITTGILSGTISAGFALADK

Q+ +LGS + KG S++G+KL+ L+ F KT+LGL+++GLLSG +A LADK
Sbjct: 197 GDQINQLGSKLQNVKGLSSLGDKLKGLSGFDKTSLGVDVSGLLSGATAALVLADK

Query: 239 GKKVAAGFELSNQVIGNVTKAISSYVLAQRVAAGLSTTGAVALITSSIMLAISPL
+KV AGFEL+NQV+GN+TKA+SSY+LAQRVAAGLS+TG VAALI S++ LAISPL
Sbjct: 257 SRKVGAGFELANQVVGNIKAVSSYILAQRVAAGLSSTGPVAALIASTVSLAISPL

Query: 299 AADKFNHANALDEFAKQFRKFGYDGDHLLAEYQRGVGTIEASLTTISTALXXXXXX
ADKFNHA +L+ +A++F+K GYDGD+LLAEYQRG GTI+AS+T I+TAL
Sbjct: 317 IADKFNHAKSLESYAERFKKLGYDGDNLLAEYQRGTGTIDASVTAINTALAAIAGG

Query: 359 XXXXXXXXPIALLVAGVTGLISGILEASKQAMFESVANRLQGKILEWEKQNGGQNY
PIALLV+G+TG+IS IL+ SKQAMFE VAN++ KI+EWEK N G+NY
Sbjct: 377 AAGSVIASPIALLVSGITGVISTILQYSKQAMFEHVANKIHNKIVEWEKNNHGKNY

Query: 419 YDSRYAAYLANNLKFLSELNKELEAERVIAITQQRWDNNIGELAGITKLGERIKSG
YD+RY A L +N+KFL LNKEL+AERVIAITQQ+WDNNIG+LAGI++LGE++ SG
Sbjct: 437 YDARYLANLQDNMKFLLNLNKELQAERVIAITQQQWDNNIGDLAGISRLGEKVLSG

Query: 479 DAFEDGKKVEAGSNITLDAKTGIIDISNSNGKKTQALHFTSPLLTTAGTESRERLTN
DAFE+GK ++A + LD+ GIID+SNS KTQ + F +PLLT GTE RER+
Sbjct: 497 DAFEEGKHLKADKLVQLDSANGIIDVSNSGAKTQHILFRTPLTPGTEHRERVQT

Query: 539 YINKLKFGRVKNWQVTDGEASSKLDTSKVIQRV-----AETEGTDEIGLIVNAK
YI KL RV +W++TDG ASS D + V+QR+ T E ++
Sbjct: 557 YITKLNINRVDSWKITDGAASSTFDLTNVVQRIGIELDNAGNVTKTETKIVAKLG

Query: 592 DIFVGQGKMNIDGGDGHDRVFYSKDGGFGNITVDGTSATEAGSYTVNRKVARGDIY
++FVG G IDGG+G+DRV YS+ G +G +T+D T TE GSYTNR V G
Sbjct: 617 NVFVGSGTTEIDGGEGYDRVHYSR-GNYGALTIDATKETEQGSYTVNRFVETGKAL

Query: 652 KRQETKVGKRTETIQYRDYELRKVGYGYQSTDNLKSVEEVIGSQFNDVKGSKFND
VG R E I+YR + + GY + D LK+VEE+IG+ ND+FKGSKFND
Sbjct: 676 STHTALVGNREEKIEYR-HSNNQHHAGYYTKDTLKAVEEIIGTSHNDIFKGSKFND

Query: 712 XXXNDVYIFRK
+ +D+++ R+
Sbjct: 735 GDGVDTIDGNDGNDRLFGGKGDDIIDGGNGDDFIDGGKGNDLLHGGKGDDIFVHRQ

Query: 772 DTLYDGTGNDKLAFADANISDIMIERTKEGIIVKRNDHSGSINI PRWY----ITSN
D + D GNDKL+F+D+N+ D+ E+ K +++ N + I W+
Sbjct: 795 DIITDSGNDKLSFSDSNLKDLTFEKVKHNLVI-TNSRKEKVTI QDWFREADFAKE

Query: 828 QSNKTDHKIEQLIGKDGSYITSXXXXXXXXXXGTVITSQELKKLADENKSQKLS
++ K D KIE++IG++G ITS IT EL K+ D + K S
Sbjct: 854 KATK-DEKIEEIIGQNGERITS--KQVDDLIAKGNGKITQDELSKVVVDNYELLKHS

Query: 888 ASSLNKLVGSMALFGTANSVSSNALQPITQPTQGI 922
+SL+KL+ S + F ++N + + P + Q +
Sbjct: 910 TNSLDKLISSASAFTSSNDSRNVLVAPTSMLDQL 944

tr Q6TB03 Leukotoxin structural protein [lktA] [Mannheimia
Q6TB03_9PAST ruminalis]

Score = 783 bits (2022), Expect = 0.0
Identities = 428/929 (46%), Positives = 588/929 (63%), Gaps = 26/9

Query: 8 KSNIQAGLNSTKGLKNLYLAIPKD--YDPQKGGLNDFIKADELGIARLAEPPN
+S QAG S K+G K + L IPKD YD +KG L D +KAA+ELGI EE N
Sbjct: 28 QSLAQAG-QSLKTGAKKIILYIPKDYQYDTEKGNGLQDLVKAAEELGIEVQKEEGN

Query: 66 AKKSVDTVNQFLSLTQTGIAISATKLEKFLQKHSTNKLAKGLDSVENIDRKLGKAS
A+ S+ T+ L LT+ GI +SA +L+K LQK K+ + + S EN+ + A
Sbjct: 87 AQTSLGTIQNVLGLTERGIVLSAPQLDKLLQK---TKVGQAIGSTENLTKGFSNAK

Query: 126 TLSSFLGTALAGIELDSLICKGDAAPDALAKASIDLNEIIGNLSQSTQTIEAFSS
+ S LG+ LAG++LD ++K ++ LAKA ++L N +I N++ S +T++AF
Sbjct: 144 GIQSILGSVLAGMDLDEALQK-NSNELTLAKAGLELTNSLIENIANSVKTLDAFGD

Query: 186 LGSTISQAKGFSNIGNKLQNLN-FSKTNLGLEIITGLLSGISAGFALADKNASTGK
LGS + KG S++G+KL+ L+ F KT+LGL++++GLLSG +A LADKNAST +
Sbjct: 203 LGSKLQNVKGLSSLGDKLKGLSGFDKTSGLDVVSGLLSGATAALVLADKNASTSR

Query: 245 GFELSNQVIGNVTKAISYYVLAQRVAAGLSTTGAVAALITSSIMLAISPLAFMNAA
GFEL+NQV+GN+TKA+SSY+LAQRVAAGLS+TG VAALI S++ LAISPLAF A
Sbjct: 263 GFELANQVVGNIKAVSSYILAQRVAAGLSSTGPVAALIASTVSLAISPLAFAGIA

Query: 305 HANALDEFQFRKFGYDGDHLLAEYQRGVGTIEASLTISTALXXXXXXXXXXXX
HA +L+ +A++F+K GYDGD+LLAEYQRG GTI+AS+T I+TAL
Sbjct: 323 HAKSLEYAERFKKLGYDGDNLLAEYQRGTGTIDASVTAINTALAAIAGGVSAAAA

Query: 365 XXPIALLVAGVTGLISGILEASKQAMFESVANRLQGKILEWEKQNGGQNYFDKGYD
PIALLV+G+TG+IS IL+ SKQAMFE VAN++ KI+EWEK N G+NYF+ GYD
Sbjct: 383 ASPIALLVSGITGVISTILQYSKQAMFEHVANKIHNKIVEWEKNNHGKNYFENGYD

Query: 425 AYLANNLKFSELNKELEAERVIAITQQRWNNIGELAGITKLGERIKSGKAYADA
A L +N+KFL LNKELEAERVIAITQQ+WDNNIG+LAGI++LGE++ SGKAY DA
Sbjct: 443 ANLQDNMKFLLNLNKELEAERVIAITQQQWDNNIGDLAGISRLGEKVLSGKAYVDA

Query: 485 KKVEAGSNITLDAKTGIIDISNSNGKKTQALHFTSPLLTAGTESRERLTNGKYSYI
K ++A + LD+ GIID+SNS KTQ + F +PLLT GTE RER+ GKY YI
Sbjct: 503 KHLKADKLVQLDSANGIIDVSNSGKAKTQHILFRTPLLTGTGKYEYI

Query: 545 FGRVKNWQVTDGEASSKLDFSKVIRQV-----AETEGTDEIGLIVNAKAGNDDI
RV +W++TDG ASS D + V+QR+ T E ++ AG+D++
Sbjct: 563 INRVDSWKITDGAASSTFDLTNVVQRIGIELDNAGNVTKTKEKIVAKLGAGDDNV

Query: 598 GKMNIIDGGDGHDRVFYSKDGGFGNITVDGTSATEAGSYTVNRKVARGDIYHEVVKR
G IDGG+G+DRV YS+ G +G +T+D T TE GSYTVNR V G HEV
Sbjct: 623 GTTEIDGGEGYDRVHYSR-GNYGALTIDATKETERGSYTVNRFVETGKALHEVTST

Query: 658 VGKRTETIQYRDYELRKVGYGYQSTDNLKSVEEVIGSQFNDVFKGSKFNDIFHSXX
VG R E I+YR + + GY + D LK+VEE+IG+ ND+FKGSKFND F+
Sbjct: 682 VGNREEKIEYR-HSNNQHHAGYYTKDTLKAVEEIIGTSHNDIFKGSKFNDAFNGGD

Query: 718 XXXXXXXXXXXXXXXXXXNXXXXXXXXXXXXXXXXXXXXXXNDVYIFRKGDGNDT
+ +D+++ R+GDGND
Sbjct: 741 IDGNDGNDRLFGGKGDDIIDGGNGDDFIDGGKGNDLLHGGKGDDIFVHRQGDGNDI

Query: 778 TGNDKLAFA DANISDIMIERTKEGIIVKRNDHSGSINI PRWY---ITSNLQNYQS
GNDKL+F+D+N+ D+ E+ K +++ N + I W+ + NY++
Sbjct: 801 DGNDKLSFSDSNLKD LT F E KV K H N L VI -TNSRKEKVTI QDW F READFAKEVP NYKA

Query: 834 HKIEQLIGKDGSYITSXXXXXXXXXGTVITSQELKKLA DENKSQKLSASDIAS
KIE++IG++G ITS IT EL K+ D + K S ++ +
Sbjct: 859 EKIEEIIIGQNGERITS--KQVDDLIAKGNGKITQDELSKVVDNYELLKHS-KNVTN

Query: 894 LVGSMALFGTANSVSSNALQPITQPTQGI 922
L+ S + F ++N + + P + Q +
Sbjct: 916 LISSASAFTSSNDSRNVLVAPTSMLDQSL 944

sp P55118 Leukotoxin (Lkt) [lktA] [Pasteurella haemolytica
LKA11_PASHA (Mannheimia
haemolytica)]

Score = 778 bits (2008), Expect = 0.0
Identities = 423/935 (45%), Positives = 587/935 (62%), Gaps = 25/9

Query: 2 SNINVIKSNIQAGLNSTKSGLKNLYLAIPKDY--DPQKGGLNDFIKAADELGIAR
 S +N ++ S K+G K + L IPKDY D +KG L D +KAA+ELGI
 Sbjct: 21 SGINRBTGOSIAKAGOSIKTGAKKTIIVPKDYQYDTEKGNGLQDIVKAAEELCIEV

Query: 60 PNHTETAKKSVDVNQFLSLTQTGIAISATKLEKFLQKHSTNKLAKGLDSVENIDR
 N A+ S+ T+ L LT+ GI +SA +L+K LQK K+ + + S EN+ +
 Sbjct: 81 GNDIAKAOTSLGTIONVILGLTERGIVLsapoLDKLQLQK---TKVGOAIGSAENLT

Query: 120 ASNVLSTLSSFEGTALAGIELDSI~~IKKGDAAPDA~~AKASIDI~~I~~NETI~~T~~GNL~~S~~OSTOT

Hit List

First Hit	Clear	Generate Collection	Print	Fwd Refs	Blkwd Refs
Generate OACs					

Search Results - Record(s) 1 through 15 of 15 returned.

1. Document ID: US 20040116363 A1

Using default format because multiple data bases are involved.

L12: Entry 1 of 15

File: PGPB

Jun 17, 2004

PGPUB-DOCUMENT-NUMBER: 20040116363

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040116363 A1

TITLE: Modified leukotoxin gene and protein

PUBLICATION-DATE: June 17, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Lo, Reggie Y.	Guelph		CA
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Lee, Raymond W	Guelph		CA
Hodgins, Doug	Milverton		CA
Strommer, Judith	Milverton		CA

US-CL-CURRENT: 514/44; 435/252.3, 435/320.1, 435/6, 435/69.1, 530/350, 536/23.7

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	TOC	Draw
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2. Document ID: US 20030065137 A1

L12: Entry 2 of 15

File: PGPB

Apr 3, 2003

DOCUMENT-IDENTIFIER: US 20030065137 A1

TITLE: Immunological methods to modulate myostatin in vertebrate subjects

CLAIMS:

46. The myostatin multimer of claim 33, wherein said multimer comprises a molecule according to the general formula (MP-X-MP)_y, wherein MP is a myostatin peptide, X is selected from the group consisting of a peptide linkage, an amino acid spacer group, a leukotoxin polypeptide and [MP].sub.n, where n is greater than or equal to 1, and y is greater than or equal to 1.

54. The myostatin immunoconjugate of claim 50, wherein the immunological carrier is a leukotoxin polypeptide.

55. The myostatin immunoconjugate of claim 51, wherein the immunological carrier is a leukotoxin polypeptide.

56. The myostatin immunoconjugate of claim 52, wherein the immunological carrier is a leukotoxin polypeptide.

57. The myostatin immunoconjugate of claim 53, wherein the immunological carrier is a leukotoxin polypeptide.

111. A recombinant vector comprising: (a) a polynucleotide according to claim 104; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

112. A recombinant vector comprising: (a) a polynucleotide according to claim 105; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

113. A recombinant vector comprising: (a) a polynucleotide according to claim 106; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

114. A recombinant vector comprising: (a) a polynucleotide according to claim 107; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

115. A recombinant vector comprising: (a) a polynucleotide according to claim 108; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

116. A recombinant vector comprising: (a) a polynucleotide according to claim 109; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

117. A recombinant vector comprising: (a) a polynucleotide according to claim 110; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	Figures	Drafter
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3. Document ID: US 6797272 B1

L12: Entry 3 of 15

File: USPT

Sep 28, 2004

DOCUMENT-IDENTIFIER: US 6797272 B1

TITLE: Enhanced immunogenicity using leukotoxin chimeras

CLAIMS:

1. A chimeric protein comprising an antigen coupled to a carrier protein, wherein said carrier protein is a leukotoxin polypeptide that activates helper T-cells and said antigen is a selected peptide hormone which is not a cytokine, and further wherein said leukotoxin polypeptide is an RTX leukotoxin from a bacterium selected from the group consisting of *Pasteurella haemolytica*, *E. coli* and *Actinobacillus pleuropneumoniae*.
2. The chimeric protein of claim 1, wherein said leukotoxin polypeptide is coupled to gonadotropin releasing hormone (GnRH) or an epitope thereof.
3. The chimeric protein of claim 2, comprising the amino acid sequence of SEQ ID NO:12.
4. The chimeric protein of claim 1, wherein the leukotoxin polypeptide is a *Pasteurella haemolytica* leukotoxin polypeptide.
5. The chimeric protein of claim 2, wherein the leukotoxin polypeptide is a *Pasteurella haemolytica* leukotoxin polypeptide.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Abstract	Chemical	Claims	DOCID	Draft
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 4. Document ID: US 6369201 B1

L12: Entry 4 of 15

File: USPT

Apr 9, 2002

DOCUMENT-IDENTIFIER: US 6369201 B1

TITLE: Myostatin multimers

CLAIMS:

5. The myostatin multimer of claim 1, wherein said myostatin immunogens are myostatin peptides and said multimer comprises a molecule according to the general formula $(MP-X-MP)^y$, wherein MP is a myostatin peptide, X is selected from the group consisting of a peptide linkage, an amino acid spacer group, a leukotoxin polypeptide and $[MP]_{\cdot sub.n}$, where n is greater than or equal to 1, and y is greater than or equal to 1.
10. The myostatin multimer of claim 9, wherein said multimer comprises six copies of SEQ ID NO:4 fused to LKT 114 as depicted in FIGS. 15A-15D (SEQ ID NO:26).
12. The myostatin multimer of claim 1, wherein said multimer comprises eight copies of SEQ ID NO:6 fused to LKT 114 as depicted in FIGS. 15A-15D (SEQ ID NO:26).

14. The myostatin multimer of claim 13, wherein said multimer comprises eight copies of SEQ ID NO:8 fused to LKT 114 as depicted in FIGS. 15A-15D (SEQ ID NO:26).

16. The myostatin multimer of claim 15, wherein said multimer comprises eight copies of SEQ ID NO:10 fused to LKT 114 as depicted in FIGS. 15A-15D (SEQ ID NO:26).

18. The myostatin multimer of claim 17, wherein said multimer comprises six copies of SEQ ID NO:12 fused to LKT 114 as depicted in FIGS. 15A-15D (SEQ ID NO:26).

20. The myostatin multimer of claim 19, wherein said multimer comprises four copies of SEQ ID NO:14 fused to LKT 114 as depicted in FIGS. 15A-15D (SEQ ID NO:26).

22. The myostatin multimer of claim 21, wherein said multimer comprises six copies of SEQ ID NO:16 fused to LKT 114 as depicted in FIGS. 15A-15D (SEQ ID NO:26).

24. The myostatin multimer of claim 23, wherein said multimer comprises four copies of SEQ ID NO:18 fused to LKT 114 as depicted in FIGS. 15A-15D (SEQ ID NO:26).

26. The myostatin multimer of claim 25, wherein said multimer comprises eight copies of SEQ ID NO:20 fused to LKT 114 as depicted in FIGS. 15A-15D (SEQ ID NO:26).

28. The myostatin multimer of claim 27, wherein said multimer comprises four copies of SEQ ID NO:22 fused to LKT 114 as depicted in FIGS. 15A-15D (SEQ ID NO:26).

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Abstract](#) | [Claims](#) | [Table](#) | [Drawings](#)

5. Document ID: US 6180112 B1

L12: Entry 5 of 15

File: USPT

Jan 30, 2001

DOCUMENT-IDENTIFIER: US 6180112 B1
TITLE: Pasteurella haemolytica vaccine

CLAIMS:

1. A whole cell vaccine composition comprising a therapeutically effective amount of recombinant Pasteurella haemolytica organism comprising an inactivated lktC gene, wherein said recombinant Pasteurella haemolytica organism expresses inactive leukotoxin, wherein and said inactive leukotoxin comprises proleukotoxin.

4. The vaccine composition of claim 1, wherein said recombinant Pasteurella haemolytica comprises an lktC::cat operon fusion.

5. The vaccine composition of claim 1, wherein said expression of inactive leukotoxin is stably maintained.

6. The vaccine composition of claim 1, wherein said recombinant Pasteurella haemolytica contains an activator for expression of said inactive leukotoxin.

8. The vaccine composition of claim 1, wherein said recombinant Pasteurella haemolytica further comprises a strong leukotoxin promoter.

9. A whole cell composition comprising recombinant *Pasteurella haemolytica* organism comprising an inactivated lktC gene, wherein said recombinant *Pasteurella haemolytica* organism expresses inactive leukotoxin, and wherein said inactive leukotoxin comprises proleukotoxin.

12. The composition of claim 9, wherein said recombinant *Pasteurella haemolytica* comprises an lktC::cat operon fusion.

13. The composition of claim 9, wherein said expression of inactive leukotoxin is stably maintained.

14. The composition of claim 9, wherein said recombinant *Pasteurella haemolytica* contains an activator for expression of said inactive leukotoxin.

16. The composition of claim 9, wherein said recombinant *Pasteurella haemolytica* further comprises a strong leukotoxin promoter.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Search](#) | [Print](#) | [Claims](#) | [DMMC](#) | [Print D...](#)

6. Document ID: US 6096320 A

L12: Entry 6 of 15

File: USPT

Aug 1, 2000

DOCUMENT-IDENTIFIER: US 6096320 A

TITLE: Vaccines with chimeric protein comprising gamma-interferon and leukotoxin derived from *Pasteurella haemolytica*

CLAIMS:

1. A vaccine composition comprising an immunogenic chimeric protein that comprises gamma-interferon (.gamma.IFN), or an active fragment thereof, linked to at least one epitope of a leukotoxin derived from *Pasteurella haemolytica*, and a pharmaceutically acceptable vehicle.
2. The vaccine composition of claim 1 wherein said chimeric protein is linked to carrier.
4. The vaccine composition of claim 1, wherein said leukotoxin is full-length P. *haemolytica* leukotoxin.
5. The vaccine composition of claim 1, wherein said leukotoxin is a truncated leukotoxin that lacks cytotoxic activity.
6. The vaccine composition of claim 5, wherein said truncated leukotoxin is LKT 352.
8. The vaccine composition of claim 7, wherein said chimeric protein comprises an amino acid sequence (a) encoded by a polynucleotide that encodes the LKT-.gamma.IFN amino acid sequence of SEQ ID NO:4, or (b) encoded by a polynucleotide that hybridizes to the polynucleotide of (a) under stringent hybridization conditions.
12. The vaccine composition of claim 8, wherein said chimeric protein comprises the LKT-.gamma.IFN amino acid sequence of SEQ ID NO:4.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Abstract	Claims	HTML	Drawn
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7. Document ID: US 5969126 A

L12: Entry 7 of 15

File: USPT

Oct 19, 1999

DOCUMENT-IDENTIFIER: US 5969126 A

TITLE: GNRH-leukotoxin chimeras

CLAIMS:

1. A DNA construct encoding a chimeric protein comprising a leukotoxin polypeptide fused to a multimer having more than one selected gonadotropin releasing hormone (GnRH) polypeptide, said DNA construct comprising a first nucleotide sequence encoding a leukotoxin polypeptide operably linked to a second nucleotide sequence encoding a GnRH multimer.
4. A DNA construct encoding a chimeric protein, wherein the chimeric protein comprises a leukotoxin polypeptide fused to first and second multimers wherein the C-terminus of the first multimer is fused to the N-terminus of the leukotoxin polypeptide and the N-terminus of the second multimer is fused to the C-terminus of the leukotoxin polypeptide, and further wherein each of said multimers comprises more than one selected gonadotropin releasing hormone (GnRH) polypeptide, said DNA construct comprising:
a first nucleotide sequence encoding the first GnRH multimer; and
a second nucleotide sequence encoding the second GnRH multimer;
wherein said first and second nucleotide sequences are operably linked by a third nucleotide sequence encoding a leukotoxin polypeptide.
12. A DNA construct encoding a chimeric protein comprising a leukotoxin polypeptide fused to a multimer having eight selected gonadotropin releasing hormone (GnRH) polypeptides, wherein the C-terminus of the leukotoxin polypeptide is fused to the N-terminus of the multimer.
13. The DNA construct of claim 12, wherein the leukotoxin polypeptide comprises the 52 kD LKT 111 carrier polypeptide, as depicted at amino acid positions 11-491, inclusive, of SEQ ID NO:10.
14. A DNA construct encoding a chimeric protein comprising a leukotoxin polypeptide fused to a multimer having eight selected gonadotropin releasing hormone (GnRH) polypeptides, wherein the C-terminus of the multimer is fused to the N-terminus of the leukotoxin polypeptide.
15. The DNA construct of claim 14, wherein the leukotoxin polypeptide comprises the 52 kD LKT 111 carrier polypeptide, as depicted at amino acid positions 11-491, inclusive, of SEQ ID NO:10.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Document ID	Claims	TOCID	Drawn D.
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8. Document ID: US 5874279 A

L12: Entry 8 of 15

File: USPT

Feb 23, 1999

DOCUMENT-IDENTIFIER: US 5874279 A

TITLE: Recombinant infectious bovine rhinotracheitis virus

CLAIMS:

7. The live recombinant infectious bovine rhinotracheitis virus of claim 1, wherein the foreign DNA encodes a polypeptide which is selected from a group consisting of Bovine Respiratory Syncytial Virus fusion protein, Bovine Respiratory Syncytial Virus attachment protein, Bovine Respiratory Syncytial Virus nucleocapsid protein, Parainfluenza type 3 fusion protein, Bovine Viral Diarrhea Virus glycoprotein 53, and P Haemolytica Leukotoxin.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Document ID	Claims	TOCID	Drawn D.
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9. Document ID: US 5849531 A

L12: Entry 9 of 15

File: USPT

Dec 15, 1998

DOCUMENT-IDENTIFIER: US 5849531 A

TITLE: Compositions and treatments for pneumonia in animals

CLAIMS:

1. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes an immunogenic *Pasteurella haemolytica* leukotoxin polypeptide, wherein said leukotoxin polypeptide has a truncation selected from the group consisting of an N-terminal truncation, a C-terminal truncation, and an N-terminal and C-terminal truncation of the native full length sequence and further wherein said leukotoxin polypeptide comprises the amino acid sequence encoded by the leukotoxin gene present in plasmid pAA342 (ATCC Accession no. 98265), or a nucleic acid molecule that hybridizes thereto under stringent conditions.

2. The nucleic acid molecule of claim 1 wherein said truncated leukotoxin is LKT 352 having an amino acid sequence as depicted at positions 11-923, inclusive, of FIGS. 5A-5F, or a nucleic acid molecule that hybridizes thereto under stringent conditions.

3. A DNA construct comprising an expression cassette comprised of:

(a) the nucleic acid molecule of claim 2; and

(b) control sequences that are operably linked to said nucleic acid molecule whereby said nucleic acid molecule can be transcribed and translated in a host cell, and further wherein at least one of said control sequences is heterologous to

: said nucleic acid molecule.

6. A DNA construct comprising an expression cassette comprised of:

(a) the nucleic acid molecule of claim 1; and

(b) control sequences that are operably linked to said nucleic acid molecule whereby said nucleic acid molecule can be transcribed and translated in a host cell, and further wherein at least one of said control sequences is heterologous to said nucleic acid molecule.

9. The nucleic acid molecule of claim 1 wherein said truncated leukotoxin is encoded by the leukotoxin gene present in plasmid pAA342.

10. A DNA construct comprising an expression cassette comprised of:

(a) the nucleic acid molecule of claim 9; and

(b) control sequences that are operably linked to said nucleic acid molecule whereby said nucleic acid molecule can be transcribed and translated in a host cell, and further wherein at least one of said control sequences is heterologous to said nucleic acid molecule.

13. The nucleic acid molecule of claim 1 wherein said truncated leukotoxin is encoded by the leukotoxin gene present in plasmid pAA101 and has an amino acid sequence as depicted at positions 1-377, inclusive, of FIG. 3.

14. A DNA construct comprising an expression cassette comprised of:

(a) the nucleic acid molecule of claim 13; and

(b) control sequences that are operably linked to said nucleic acid molecule whereby said nucleic acid molecule can be transcribed and translated in a host cell, and further wherein at least one of said control sequences is heterologous to said nucleic acid molecule.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Abstracts	Chemical	Claims	TOC	Drawn
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10. Document ID: US 5837268 A

L12: Entry 10 of 15

File: USPT

Nov 17, 1998

DOCUMENT-IDENTIFIER: US 5837268 A

TITLE: GnRH-leukotoxin chimeras

CLAIMS:

1. A chimeric protein comprising a leukotoxin polypeptide fused to first and second multimers, wherein the C-terminus of the first multimer is fused to the N-terminus of the leukotoxin polypeptide and the N-terminus of the second multimer is fused to the C-terminus of the leukotoxin polypeptide, and further wherein each of said multimers comprises more than one selected GnRH polypeptide.

2. The chimeric protein of claim 1 wherein the first and second GnRH multimers are different and comprise molecules according to the general formula [GnRH-X-GnRH]._n, wherein:

GnRH comprises a GnRH polypeptide;

X is selected from the group consisting of a peptide linkage, an amino acid spacer group and a leukotoxin polypeptide; and

n is an integer greater than or equal to 1.

3. The chimeric protein of claim 1 wherein the first and second GnRH multimers are the same and comprise molecules according to the general formula [GnRH-X-GnRH]._n, wherein:

GnRH comprises a GnRH polypeptide;

X is selected from the group consisting of a peptide linkage, an amino acid spacer group and a leukotoxin polypeptide; and

n is an integer greater than or equal to 1.

4. The chimeric protein of claim 3 wherein X is an amino acid spacer group having at least one helper T-cell epitope.

5. The chimeric protein of claim 3 wherein n is 4.

6. The chimeric protein of claim 1 wherein the leukotoxin polypeptide lacks cytotoxic activity.

7. The chimeric protein of claim 6 wherein the leukotoxin polypeptide is the polypeptide depicted at amino acid residues 11-923 of SEQ ID NO:6.

8. The chimeric protein of claim 6 wherein the leukotoxin polypeptide is the polypeptide depicted at amino acid residues 11-491 of SEQ ID NO:10.

9. The chimeric protein of claim 6 wherein the leukotoxin polypeptide is SEQ ID NO:17.

10. The chimeric protein of claim 3 wherein the first multimer further comprises the amino acid sequence (Met-Ala-Thr-Val-Ile-Asp-Ser SEQ ID NO:21) fused to the N-terminus thereof.

11. The chimeric protein of claim 1 comprising the amino acid sequence depicted in FIGS. 9-1 through 9-6 (SEQ ID NO:15 and SEQ ID NO:16).

12. A vaccine composition comprising the chimeric protein of claim 1 and a pharmaceutically acceptable vehicle.

13. A vaccine composition comprising the chimeric protein of claim 3 and a pharmaceutically acceptable vehicle.

14. A vaccine composition comprising the chimeric protein of claim 5 and a pharmaceutically acceptable vehicle.

15. A vaccine composition comprising the chimeric protein of claim 6 and a pharmaceutically acceptable vehicle.

16. A vaccine composition comprising the chimeric protein of claim 11 and a pharmaceutically acceptable vehicle.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Abstract	Chemical	Claims	FIGNC	Drawn
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11. Document ID: US 5723129 A

L12: Entry 11 of 15

File: USPT

Mar 3, 1998

DOCUMENT-IDENTIFIER: US 5723129 A

TITLE: GnRH-leukotoxin chimeras

CLAIMS:

1. A chimeric protein comprising a leukotoxin polypeptide fused to a multimer having more than one selected GnRH polypeptide, whereby said leukotoxin portion of said chimeric protein acts to increase the immunogenicity of said GnRH multimer.
2. The chimeric protein of claim 1 wherein said leukotoxin polypeptide lacks leukotoxic activity.
3. The chimeric protein of claim 2 wherein said leukotoxin is LKT 352.
4. The chimeric protein of claim 2 wherein said leukotoxin is LKT 111.
5. The chimeric protein of claim 1 wherein said GnRH multimer comprises a molecule according to the general formula GnRH-X-GnRH wherein X is selected from the group consisting of a peptide linkage, an amino acid spacer group, a leukotoxin polypeptide and [GnRH].sub.n where n is greater than or equal to 1, and further wherein GnRH comprises any GnRH polypeptide.
6. The chimeric protein of claim 5 wherein X comprises an amino acid spacer group including at least one helper T-cell epitope.
7. The chimeric protein of claim 1 wherein said chimeric protein comprises the amino acid sequence depicted in FIGS. 5A-5h, SEQ ID NOS:7-8.
8. The chimeric protein of claim 1 wherein said chimeric protein comprises the amino acid sequence depicted in FIGS. 7A-7E, SEQ ID NOS:9-10.
9. A vaccine composition comprising the chimeric protein of claim 1 and a pharmaceutically acceptable vehicle.
10. A vaccine composition comprising the chimeric protein of claim 2 and a pharmaceutically acceptable vehicle.
11. A vaccine composition comprising the chimeric protein of claim 5 and a pharmaceutically acceptable vehicle.
12. A vaccine composition comprising the chimeric protein of claim 7 and a pharmaceutically acceptable vehicle.
13. A vaccine composition comprising the chimeric protein of claim 8 and a pharmaceutically acceptable vehicle.

19. A chimeric protein comprising a leukotoxin polypeptide fused to a multimer having eight selected GnRH polypeptides, wherein the C-terminus of the leukotoxin polypeptide is fused to the N-terminus of the multimer.

20. The chimeric protein of claim 19, wherein the leukotoxin polypeptide comprises the 52 kD LKT 111 carrier polypeptide.

21. A chimeric protein comprising a leukotoxin polypeptide fused to a multimer having eight selected GnRH polypeptides, wherein the C-terminus of the multimer is fused to the N-terminus of the leukotoxin polypeptide.

22. The chimeric protein of claim 21, wherein the leukotoxin polypeptide comprises the 52 kD LKT 111 carrier polypeptide.

23. A vaccine composition comprising the chimeric protein of claim 19 and a pharmaceutically acceptable vehicle.

24. A vaccine composition comprising the chimeric protein of claim 20 and a pharmaceutically acceptable vehicle.

25. A vaccine composition comprising the chimeric protein of claim 21 and a pharmaceutically acceptable vehicle.

26. A vaccine composition comprising the chimeric protein of claim 22 and a pharmaceutically acceptable vehicle.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Abstract](#) | [Claims](#) | [EPOC](#) | [Dram](#) |

12. Document ID: US 5708155 A

L12: Entry 12 of 15

File: USPT

Jan 13, 1998

DOCUMENT-IDENTIFIER: US 5708155 A

TITLE: Enhanced immunogenicity using leukotoxin chimeras

CLAIMS:

1. A DNA construct encoding a chimeric protein, said DNA construct comprising a first nucleotide sequence encoding a leukotoxin polypeptide capable of activating helper T-cells directed to a selected antigen, operably linked to a second nucleotide sequence encoding said selected antigen.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Abstract](#) | [Claims](#) | [EPOC](#) | [Dram](#) |

13. Document ID: US 5594107 A

L12: Entry 13 of 15

File: USPT

Jan 14, 1997

DOCUMENT-IDENTIFIER: US 5594107 A
** See image for Certificate of Correction **
TITLE: Chimeric protein comprising an RTX-family cytotoxin and interferon-2 or interferon

CLAIMS:

1. An immunogenic chimeric protein comprising a cytokine selected from the group consisting of interleukin-2 (IL2), and gamma-interferon (.gamma.IFN), linked to at least one epitope of an RTX cytotoxin which comprises the amino acid sequence Gly-Gly-X-Gly-(Asn or Asp)-Asp (SEQ ID NO: 5), wherein X is selected from the group consisting of an aliphatic amino acid, and a charged amino acid or its corresponding neutral amino acid.
2. The chimeric protein of claim 1 wherein X is selected from the group consisting of Lys, Asp, Val, and Asn.
3. The chimeric protein of claim 1 wherein said RTX cytotoxin is a leukotoxin.
4. The chimeric protein of claim 3 wherein said leukotoxin is derived from *P. haemolytica*.
5. The chimeric protein of claim 4 wherein said leukotoxin is full-length *P. haemolytica* leukotoxin.
6. The chimeric protein of claim 3 wherein said leukotoxin is a truncated leukotoxin which lacks leukotoxic activity.
7. The chimeric protein of claim 6 wherein said truncated leukotoxin is LKT 352.
8. The chimeric protein of claim 1 wherein said cytokine is interleukin-2 (IL2), or an active fragment thereof.
9. The chimeric protein of claim 8 wherein said IL2 is bovine IL2, or an active fragment thereof.
10. The chimeric protein of claim 9 comprising the amino acid sequence depicted in FIG. 3 (SEQ ID NOS: 1-2).
11. The chimeric protein of claim 1 wherein said cytokine is gamma-interferon (.gamma.IFN), or an active fragment thereof.
12. The chimeric protein of claim 11 wherein said .gamma.IFN is bovine .gamma.IFN, or an active fragment thereof.
13. The chimeric protein of claim 12 comprising the amino acid sequence depicted in FIG. 7 (SEQ ID NOS: 3-4).

Full	Title	Citation	Front	Review	Classification	Date	Reference	Image	Image	Claims	EDOC	Drawn
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14. Document ID: US 5422110 A

L12: Entry 14 of 15

File: USPT

Jun 6, 1995

DOCUMENT-IDENTIFIER: US 5422110 A

TITLE: Enhanced immunogenicity using leukotoxin chimeras

CLAIMS:

1. An immunological carrier system comprising a chimeric protein, said chimeric protein consisting of a leukotoxin molecule which lacks leukotoxic activity, fused to somatostatin (SRIF), whereby said leukotoxin of said chimeric protein acts to increase the immunogenicity of said SRIF.
5. An immunological carrier system comprising a chimeric protein, said chimeric protein consisting of a leukotoxin molecule which lacks leukotoxic activity, fused to gonadotropin releasing hormone (GnRH), whereby said leukotoxin of said chimeric protein acts to increase the immunogenicity of said GnRH.
6. The carrier system of claim 5 wherein said chimeric protein consists of the amino acid sequence depicted in FIG. 8 (SEQ ID NO:9).
7. A vaccine composition comprising the chimeric protein of claim 5 and a pharmaceutically acceptable vehicle.
9. An immunological carrier system comprising a chimetic protein, said chimetic protein consisting of a leukotoxin molecule which lacks leukotoxic activity, fused to bovine rotavirus VP4, whereby said leukotoxin of said chimeric protein acts to increase the immunogenicity of said VP4.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	TOC	Frame
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15. Document ID: US 5273889 A

L12: Entry 15 of 15

File: USPT

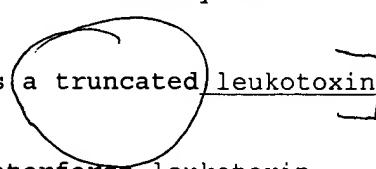
Dec 28, 1993

DOCUMENT-IDENTIFIER: US 5273889 A

** See image for Certificate of Correction **

TITLE: Gamma-iterferon-leukotoxin gene fusions and uses thereof

CLAIMS:

1. A DNA construct comprising a first nucleotide sequence encoding gamma-interferon (.gamma.IFN), operably linked to a second nucleotide sequence encoding an immunogenic leukotoxin, wherein said leukotoxin is characterized by having the amin acid sequence G-G-X-G-X-D (SEQ ID NO. 3) where X is K, D, V or N.
4. The DNA construct of claim 1 wherein said leukotoxin is a P. haemolytica leukotoxin.
5. The DNA construct of claim 1 wherein said leukotoxin is a truncated leukotoxin as present in plasmid pAA352 (ATCC Accession No. 68283). 
7. A vector comprising a DNA construct encoding a gamma-interferon-leukotoxin fusion protein, wherein the plasmid is pAA497.

1: Microbiology. 1996 Sep;142 (Pt 9):2499-507.

[Related Articles](#), [Links](#)

Characterization of epitopes involved in the neutralization of *Pasteurella haemolytica* serotype A1 leukotoxin.

Lainson FA, Murray J, Davies RC, Donachie W.

Moredun Research Institute, Edinburgh, UK.

Defined segments of the leukotoxin A gene (*lktA*) from an A1 serotype of *Pasteurella haemolytica* were cloned into a plasmid vector and expressed as LacZ alpha fusion proteins. These fusion proteins were electrophoresed in SDS-PAGE gels and their immunoblotting reactivities with several monoclonal antibodies characterized. The epitope recognized by a strongly neutralizing monoclonal antibody was localized to a 32 amino acid region near the C terminus of the leukotoxin A (*LktA*) molecule. The epitope recognized by a non-neutralizing antibody was localized to a 33 amino acid region immediately adjacent. Smaller recombinant peptides containing these epitopes were not antigenic, but a polypeptide encompassing 229 amino acids at the C terminus evoked neutralizing antibodies when used to immunize specific-pathogen-free lambs. The distributions of linear epitopes recognized by this antiserum and by antisera raised to full-length recombinant *LktA* and to native *LktA* produced by *P. haemolytica* serotype A1 were determined by their reactivities with a set of overlapping 10 amino acid synthetic peptides. This revealed a complex distribution of linear epitopes at the C-terminal end of *LktA*. Toxin-neutralizing antibodies in convalescent sheep serum were shown to be directed against conformational epitopes by selective absorption of antibodies directed against linear epitopes.

PMID: 8828217 [PubMed - indexed for MEDLINE]

DOCUMENT-IDENTIFIER: US 5969126 A

TITLE: GNRH-leukotoxin Chimeras

CLAIMS:

1. A DNA construct encoding a chimeric protein comprising a leukotoxin polypeptide fused to a multimer having more than one selected gonadotropin releasing hormone (GnRH) polypeptide, said DNA construct comprising a first nucleotide sequence encoding a leukotoxin polypeptide operably linked to a second nucleotide sequence encoding a GnRH multimer.
4. A DNA construct encoding a chimeric protein, wherein the chimeric protein comprises a leukotoxin polypeptide fused to first and second multimers wherein the C-terminus of the first multimer is fused to the N-terminus of the leukotoxin polypeptide and the N-terminus of the second multimer is fused to the C-terminus of the leukotoxin polypeptide, and further wherein each of said multimers comprises more than one selected gonadotropin releasing hormone (GnRH) polypeptide, said DNA construct comprising:
 - a first nucleotide sequence encoding the first GnRH multimer; and
 - a second nucleotide sequence encoding the second GnRH multimer;wherein said first and second nucleotide sequences are operably linked by a third nucleotide sequence encoding a leukotoxin polypeptide.
12. A DNA construct encoding a chimeric protein comprising a leukotoxin polypeptide fused to a multimer having eight selected gonadotropin releasing hormone (GnRH) polypeptides, wherein the C-terminus of the leukotoxin polypeptide is fused to the N-terminus of the multimer.
13. The DNA construct of claim 12, wherein the leukotoxin polypeptide comprises the 52 kD LKT 111 carrier polypeptide, as depicted at amino acid positions 11-491, inclusive, of SEQ ID NO:10.
14. A DNA construct encoding a chimeric protein comprising a leukotoxin polypeptide fused to a multimer having eight selected gonadotropin releasing hormone (GnRH) polypeptides, wherein the C-terminus of the multimer is fused to the N-terminus of the leukotoxin polypeptide.
15. The DNA construct of claim 14, wherein the leukotoxin polypeptide comprises the 52 kD LKT 111 carrier polypeptide, as depicted at amino acid positions 11-491, inclusive, of SEQ ID NO:10.

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In case of problems, please read the online BLAST help.
If your question is not covered, please contact <helpdesk@expasy.org>.

NCBI BLAST program reference [PMID:9254694] :

Altschul S.F., Madden T.L., Schäffer A.A., Zhang J., Zhang Z., Miller W., Lipman D.J. Gapped BLAST and PSI-BLAST: a new generation of protein database search programs. Nucleic Acids Res. 25:3389-3402(1997).

Query: 927 AA (of which 8% low-complexity regions filtered out)

Date run: 2006-03-27 16:58:36 UTC+0100 on blast01.vital-it.ch

Program: NCBI BLASTP 2.2.13 [Nov-27-2005]

Database: UniProtKB

2,893,171 sequences; 943,878,704 total letters

UniProt Knowledgebase Release 7.3 consists of:

UniProtKB/Swiss-Prot Release 49.3 of 21-Mar-2006: 212425 entries

UniProtKB/TrEMBL Release 32.3 of 21-Mar-2006: 2666963 entries

List of potentially matching sequences

Send selected sequences to

Include query sequence

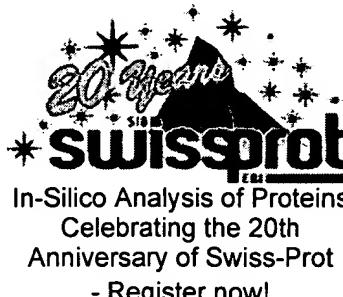
Db	AC	Description
----	----	-------------

- tr Q93GI2 _MORBO RTX toxin [mbxA] [Moraxella bovis]
- sp Q9ETX2 LKTA_MANGL Leukotoxin (Lkt) [lktA] [Mannheimia glucosidase]

- tr Q6TB03 _9PAST Leukotoxin structural protein [lktA] [Mannheimia
- sp P55118 LKA11_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
- sp Q7BHI8 LKA1B_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
- sp P16535 LKA1A_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
- sp P0C083 LKTA6_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
- sp P0C084 LKA7A_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
- sp Q9EV29 LKA2D_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
- sp Q9EV32 LKA16_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
- sp Q9EV34 LKTA8_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
- sp Q9EV33 LKA14_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
- sp Q9EV31 LKA13_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
- sp P0C085 LKA7B_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
- sp Q9EV27 LKA2E_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
- sp Q9EV30 LKA2A_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
- sp P0C082 LKA2C_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
- sp P0C081 LKA2B_PASHA Leukotoxin (Lkt) [lktA] [Pasteurella haemo.
- sp P55123 LKTA_PASSP Leukotoxin (PLLkt) [lktA] [Pasteurella haem.
- sp P55117 LKTA_PASTR Leukotoxin (Lkt) [lktA] [Pasteurella trehal.
- tr Q5DI89 _9PAST ApxIIA [apxIIA] [Actinobacillus porcitonsillarum
- tr Q84C02 _ACTPL ApxIIA [Actinobacillus pleuropneumoniae (Haemoph
- sp P15377 RTX2A_ACTPL RTX-II toxin determinant A (APX-IIA) (Hemo.
- tr Q93NP1 _ACTPL RTX toxin IIIA [Actinobacillus pleuropneumoniae (
- tr Q5XUT6 _ACTPL ApxIIA [apxIIA] [Actinobacillus pleuropneumoniae
- sp Q00951 HLYA_ACTSU Hemolysin (Cytolysin II) (CLY-IIA) (HLY-IIA.
- tr Q8KWZ6 _ACTEU AqxA [aqxA] [Actinobacillus equuli]
- tr Q8KWZ9 _9PAST AqxA [aqxA] [Actinobacillus cf. equuli]
- sp Q9RCG8 PAXA_PASAE Exotoxin paxA [paxA] [Pasteurella aerogenes]
- tr Q93NP0 _ACTPL RTX-toxin IIIA [Actinobacillus pleuropneumoniae
- sp P55131 RTX32_ACTPL RTX-III toxin determinant A from serotype .
- sp P55130 RTX31_ACTPL RTX-III toxin determinant A from serotype .
- tr Q6TB11 _9PAST Leukotoxin structural protein (Fragment) [lktA]
- tr Q6TB07 _9PAST Leukotoxin structural protein (Fragment) [lktA]
- tr Q8FE01 _ECOL6 Hemolysin A [hlyA] [Escherichia coli O6]
- tr Q8GA40 _ECOLI Hemolysin A [hlyA] [Escherichia coli]
- tr Q8G9Z4 _ECOLI HlyA protein [hlyA] [Escherichia coli]
- sp P09983 HLYAC_ECOLI Hemolysin, chromosomal [hlyA] [Escherichia.
- sp P08715 HLYAP_ECOLI Hemolysin, plasmid [hlyA] [Escherichia coli]
- tr Q548V0 _ACTPL ApxIA [apxIA] [Actinobacillus pleuropneumoniae (
- tr Q93NP2 _ACTPL RTX toxin IA [Actinobacillus pleuropneumoniae (H
- tr Q3ZU04 _ECOLI Hemolysin A [ehxA] [Escherichia coli]
- tr O85101 _ECOLI Hemolysin [ehxA] [Escherichia coli]
- tr Q9LC58 _ECOLI Hemolysin A [EHEC-hlyA] [Escherichia coli]

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[\[Keywords\]](#) [\[Features\]](#) [\[Sequence\]](#) [\[Tools\]](#)

Note: most headings are clickable, even if they don't appear as links. They link to the user manual or other documents.

Entry information

Entry name	LKA11_PASHA	
Primary accession number	P55118	
Secondary accession numbers	None	
Integrated into Swiss-Prot on	October 1, 1996	
Sequence was last modified on	October 1, 1996 (Sequence version 1)	
Annotations were last modified on	March 21, 2006 (Entry version 39)	

Name and origin of the protein

Protein name	Leukotoxin	
Synonym	Lkt	
Gene name	Name: IktA	
From	Pasteurella haemolytica (Mannheimia haemolytica)	[TaxID: 75985]
Taxonomy	Bacteria; Proteobacteria; Gammaproteobacteria; Pasteurellales; Pasteurellaceae; Mannheimia.	

References

[1] NUCLEOTIDE SEQUENCE [GENOMIC DNA].

STRAIN=Serotype A11;
 PubMed=8225575 [NCBI, ExPASy, EBI, Israel, Japan]
 Burrows L.L., Olah-Winfield E., Lo R.Y.C.;
 "Molecular analysis of the leukotoxin determinants from Pasteurella haemolytica serotype 16.";
Infect. Immun. 61:5001-5007(1993).

Comments

- **FUNCTION:** Pasteurella leukotoxins are exotoxins that attack host leukocytes and especially polymorphonuclear cells, by causing cell rupture. The leukotoxin binds to the host LFA-integrin and induces a signaling cascade leading to many biological effects, including tyrosine phosphorylation of the CD18 tail, elevation of the intracellular Ca(2+) and lysis

host cell (*By similarity*). This leukotoxin is a major contributor to the pathogenesis of lung injury in ovine pneumonic pasteurellosis. It has also weak hemolytic activity.

- **SUBCELLULAR LOCATION:** Secreted protein (*By similarity*).
- **DOMAIN:** The transmembrane domains are believed to be involved in pore formation in target cells (*By similarity*).
- **DOMAIN:** The Gly-rich region is probably involved in calcium binding, which is required for target cell-binding and cytolytic activity (*By similarity*).
- **DOMAIN:** The C-terminal domain contains an export signal that is recognized by the ABC transporter complex IktBD (*By similarity*).
- **PTM:** Acylated by IktC. The toxin only becomes active when modified (*By similarity*).
- **MISCELLANEOUS:** The IktCABD operon has a complex mosaic structure that has been derived by extensive inter- and intraspecies horizontal DNA transfer and intragenic recombination events.
- **SIMILARITY:** Belongs to the RTX prokaryotic toxin (TC 1.C.11) family [view classification]
- **SIMILARITY:** Contains 5 hemolysin-type calcium-binding repeats.

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Cross-references

Sequence databases

EMBL	U01215; AAB36689.1; -; Unassigned_DNA.	[EMBL / GenBank / DDBJ] [CoCodingSequence]
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3D structure databases

ModBase P55118.

Protein-protein interaction databases

DIP P55118.

2D gel databases

SWISS-2DPAGE Get region on 2D PAGE.

Organism-specific gene databases

HOGENOM [Family / Alignment / Tree]

Family and domain databases

InterPro	IPR001343; Hemlysn_Ca_bd. IPR003995; RtxA. IPR011049; Serralysn_like_C. Graphical view of domain structure. PF00353; HemolysinCabind; 5.
Pfam	PF02382; RTX; 1. Pfam graphical view of domain structure.
PRINTS	PR00313; CABNDNGRPT. PR01488; RTXTOXINA.
PROSITE	PS00330; HEMOLYSIN_CALCIUM; 4.
ProDom	[Domain structure / List of seq. sharing at least 1 domain]
BLOCKS	P55118.

Other

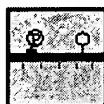
ProtoNet P55118.

UniRef View cluster of proteins with at least 50% / 90% / 100% identity.

Keywords

Calcium; Cytolysis; Hemolysis; Lipoprotein; Membrane; Repeat; Toxin; Transmembrane; Virulence.

Features



Feature table viewer



Feature aligner

Key	From	To	Length	Description	FTId
CHAIN	1	953	953	Leukotoxin.	PRO_0000196230
TRANSMEM	230	250	21	Potential.	
TRANSMEM	297	317	21	Potential.	
TRANSMEM	381	401	21	Potential.	
REPEAT	715	732	18	Hemolysin-type calcium-binding 1.	
REPEAT	733	750	18	Hemolysin-type calcium-binding 2.	
REPEAT	751	768	18	Hemolysin-type calcium-binding 3.	
REPEAT	769	786	18	Hemolysin-type calcium-binding 4.	
REPEAT	789	806	18	Hemolysin-type calcium-binding 5.	

Sequence information

Length: 953 AA [This is the length of the unprocessed precursor]

Molecular weight: 102206 Da
[This is the MW of the unprocessed precursor]

CRC64: 927FF56CFC884F12
is a checksum on the sequence

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70	80	90	100	110	120
GLQDLVKAAE	ELGIEVQKEE	GNDIAKAQTS	LGTIQNVLGL	TERGIVLSAP	QLDKLLQKTK
130	140	150	160	170	180
VGQQAIGSAEN	LTKGFSNAKT	VLSGIQSILG	SVLAGMDLDE	ALQKNSNELT	LAKAGLELTN
190	200	210	220	230	240
SLIENIANSV	KTLDAGFDQI	NQLGSKLQNV	KGLSSLGDKL	KGLSGFDKTS	LG LDVVSGLL
250	260	270	280	290	300
SGATAALVIA	DKNASTSRKV	GAGFELANQV	VGNITKAVSS	YILAQRVAAG	LSSTGPVAAL
310	320	330	340	350	360
IASTVSLAIS	PLAFAGIADK	FNHAKSLESY	AERFKKLGYD	GDNLLAEYQR	GTGTIDRSVT
370	380	390	400	410	420
AINATALAAIA	GGVSAAGRGS	VIASPIALLV	SGITGVISTI	LQYSKQAMFE	H VANKIHNKI
430	440	450	460	470	480
VEWEKNNHGK	NYFENGYDAR	YLANLQDNMK	FLLNLNKELO	AERVIAITQQ	QWDNNIGDLA

490 500 510 520 530 540
 GISRLGEKVL SGKAYVDAFE EGKHLKADKL VQLDSANGII DVSNSGAKT QDILFRTPLL
 550 560 570 580 590 600
 TPGTDDRERV QTGKYEYITK LNINRVDSWK ITDGAASSTF DLTNVVQRIG IELDNAGNVT
 610 620 630 640 650 660
 KTKETKIVAK LGAGDDNVFV GSGTTEIDGG EGYDRVHYSR GNYGALTIDA TKETEQGSYT
 670 680 690 700 710 720
 VNRFVETGKA LHEGTSTHTA LVGNREEKIE YRHSNNQHHA GYYTKDTLKA VEEIIGTSHN
 730 740 750 760 770 780
 DIFKGSKFND AFNNGGDGVDT IDGKDGNDRD FGGKGDDIID GGNNGDDFIDG GKGNNDLLHGG
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 KGDDIFVHRQ GDGNDIITDS DGNDKLSFSD SNLKDLTKEK VKHNLVITNS RKEKVTIQDW
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 FREADFAKEV RNYKATKDEK IEEIIGQNGE RITSKVDDL IAKGNGKITQ DELSKVVDNY
 910 920 930 940 950
 ELLKHSKNVT NSLDKLISSA SAFTSSNDSR NVLVAPTSML DQSLSSLQFA RAA

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Sequence analysis tools: ProtParam,
ProtScale, Compute pI/Mw, PeptideMass,
PeptideCutter, Dotlet (Java)

 ScanProsite, MotifScan



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DATE: Monday, March 27, 2006

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<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR</i>			
		(pasteurell\$ or leukotoxin or lkt or hemolytica or haemolytica).clm. and (fusion	
<input type="checkbox"/>	L1	or recombinant or his6 or 6his to histag or his-tag or 6x or hishishishishis).clm.	94
<input type="checkbox"/>	L2	rtx.clm. same fusion.clm.	1
<input type="checkbox"/>	L3	l1 and amalose	0
<input type="checkbox"/>	L4	l1 and xa	4
<input type="checkbox"/>	L5	fusion and xa and (leukotoxin or rtx or lkt or moraxella or pasteurella)	598
<input type="checkbox"/>	L6	fusion same(leukotoxin or rtx or lkt or moraxella or pasteurella)	174
<input type="checkbox"/>	L7	L6 and xa	28
<input type="checkbox"/>	L8	l1 and (hexahistidine or nickel or chelate or ninta or ni-nta or metal or 6his or hishishis)	42
<input type="checkbox"/>	L9	l6 and (hexahistidine or nickel or chelate or ninta or ni-nta or metal or 6his or hishishis)	78
<input type="checkbox"/>	L10	l6 same (hexahistidine or nickel or chelate or ninta or ni-nta or metal or 6his or hishishis)	1
<input type="checkbox"/>	L11	leukotoxi\$.clm.	49
<input type="checkbox"/>	L12	L11 and (fused or fusion or chimeric or heterologous or singlechain or single- chain).clm.	15

END OF SEARCH HISTORY

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HETEROLOGOU	5
SINGLECHAIN	20
SINGLECHAINS	2
SINGLE-CHAIN	13354
(L11 AND (FUSED OR FUSION OR CHIMERIC OR HETEROLOGOUS OR SINGLECHAIN OR SINGLE-CHAIN).CLM.).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	15

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1: Mol Microbiol. 1993 Jan;7(2):285-8.

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Q pili enhance the attachment of *Moraxella bovis* to bovine corneas in vitro.

Ruehl WW, Marrs C, Beard MK, Shokooki V, Hinojoza JR, Banks S, Bieber D, Mattick JS.

Department of Pathology, Stanford University School of Medicine, California.

Moraxella bovis, the causative agent of infectious bovine keratoconjunctivitis, exhibits several virulence factors, including pili, haemolysin, leukotoxin, and proteases. The pili are filamentous appendages which mediate bacterial adherence. Prior studies have shown that Q-piliated *M. bovis* Epp63 are more infectious and more pathogenic than I-piliated and non-piliated isogenic variants, suggesting that Q pili per se, or traits associated with Q-pilin expression, promote the early association of Q-piliated bacteria with bovine corneal tissue. In order to better evaluate the role of Q pili in *M. bovis* attachment, several *M. bovis* strains and a recombinant *P. aeruginosa* strain which elaborates *M. bovis* Q pili but not *P. aeruginosa* PAK pili, were evaluated using an in vitro corneal attachment assay. For each strain tested, pilated organisms attached better than non-piliated bacteria. *M. bovis* Epp63 Q-piliated bacteria adhered better than either the I-piliated or non-piliated isogenic variants. Finally, recombinant *P. aeruginosa* organisms elaborating *M. bovis* Q pili adhered better than the parent *P. aeruginosa* strain which did not produce *M. bovis* pili. These results indicate that the presence of pili, especially Q pili, enhances the attachment of bacteria to bovine cornea in vitro.

PMID: 8095318 [PubMed - indexed for MEDLINE]

Infect. Immun., Dec 1993, 5001-5007, Vol 61, No. 12
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Molecular analysis of the leukotoxin determinants from *Pasteurella haemolytica* serotypes 1 to 16

LL Burrows, E Olah-Winfield and RY Lo

Department of Microbiology, University of Guelph, Ontario, Canada.

All sixteen serotypes of *Pasteurella haemolytica* were shown to produce a leukotoxin protein which is immunologically related to the well-characterized serotype 1 leukotoxin. All of the leukotoxins were weakly hemolytic and were able to bind to BL-3 target cells. The leukotoxin determinants were characterized by Southern blot hybridization by use of the previously cloned serotype 1 determinant as the probe, and a number of distinct classes were identified. The leukotoxin determinants from serotypes 2, 3, and 11 were cloned. Nucleotide sequence analysis of the lktC and lktA genes of the serotype 3 and 11 determinants revealed nucleotide substitutions throughout the coding sequences. A comparison of the lktC and lktA genes and deduced proteins of serotypes 1, 3, and 11 showed that they are highly homologous.

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L12: Entry 2 of 15

File: PGPB

Apr 3, 2003

DOCUMENT-IDENTIFIER: US 20030065137 A1

TITLE: Immunological methods to modulate myostatin in vertebrate subjects

CLAIMS:

46. The myostatin multimer of claim 33, wherein said multimer comprises a molecule according to the general formula (MP-X-MP)_y, wherein MP is a myostatin peptide, X is selected from the group consisting of a peptide linkage, an amino acid spacer group, a leukotoxin polypeptide and [MP].sub.n, where n is greater than or equal to 1, and y is greater than or equal to 1.

54. The myostatin immunoconjugate of claim 50, wherein the immunological carrier is a leukotoxin polypeptide.

55. The myostatin immunoconjugate of claim 51, wherein the immunological carrier is a leukotoxin polypeptide.

56. The myostatin immunoconjugate of claim 52, wherein the immunological carrier is a leukotoxin polypeptide.

57. The myostatin immunoconjugate of claim 53, wherein the immunological carrier is a leukotoxin polypeptide.

111. A recombinant vector comprising: (a) a polynucleotide according to claim 104; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

112. A recombinant vector comprising: (a) a polynucleotide according to claim 105; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

113. A recombinant vector comprising: (a) a polynucleotide according to claim 106; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

114. A recombinant vector comprising: (a) a polynucleotide according to claim 107; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

115. A recombinant vector comprising: (a) a polynucleotide according to claim 108; and (b) control elements that are operably linked to said polynucleotide whereby a

coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

116. A recombinant vector comprising: (a) a polynucleotide according to claim 109; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

117. A recombinant vector comprising: (a) a polynucleotide according to claim 110; and (b) control elements that are operably linked to said polynucleotide whereby a coding sequence within said polynucleotide can be transcribed and translated in a host cell, and at least one of said control elements is heterologous to said coding sequence.

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CLUSTAL FORMAT for T-COFFEE Version_1.37, CPU=0.04 sec, SCORE=22400, Nseq=2, Len=964

unk|VIRT10457|Blast_submission sp|P55118|LKA11_PASHA -----MSNINVIKSNIQAGLNST-----KSGLKNLYLAIPKDY MGNKLTNISTNLKSSWLTAKSGLNRTGQSLAKAGQSLKTGAKKIILYIPKDY :*:.. . :**** * * * * : * ****

unk|VIRT10457|Blast_submission sp|P55118|LKA11_PASHA TLNDFIKAADELGIAIRLAEPPNHETAKSVDTVNQFLSLTQTGIAISATKL GLQDLVKAAELGIEVQKEEGNDIAKAQTSGLTIQNVLGLTERGIVLSAPQL *.*:****:**** ** *. . *.*:.*:.*:.*:.*: *.*:.*:.*:

unk|VIRT10457|Blast_submission sp|P55118|LKA11_PASHA TNKLAKGLDSENVIDRKLGKASNVLSTLSSFLGTALAGIELDSLICKGDAAP -TKVGQAIAGSAENLTKGSNAKTVLSGIQSILGSVLAGMDLDEALQK-NSNE .*:...*.**: : :.*:**** :.*:****:****:****. :* :

unk|VIRT10457|Blast_submission sp|P55118|LKA11_PASHA DLNEIIGNLSQSTQTIEAFSSQLAKLGSTISQAKGFSNIGNKLQNLN-FSK ELTNSLIENIANSVKTLDAFGDQINQLGSKLQNVKGLSSLGDKLKGDFDK :* *.:* *::*.:*::*..*: :****.:.:.****:.*:****:.*. **

unk|VIRT10457|Blast_submission sp|P55118|LKA11_PASHA TGLLSGISAGFALADKNASTGKKVAAGFELSNQVIGNVTKAISSYVLAQRVA SGLLSGATAALVLADKNASTSRKVVGAGFELANQVVGNIITKAVSSYILAQRVA :***** :*:.*****.**:.*.*****:***:***:***:***:*****

unk|VIRT10457|Blast_submission sp|P55118|LKA11_PASHA VAALITSSIMLAISPLAFMNAADKFHNHALDEFAKQFRKFGYDGDHLLAELY VAALIASTVSLAISPLAFAGIADKFHNHAKSLESYAERFKKLGDFDNLLAELY *****:*: :*****. . *****:****:****:****:****:****:****

unk|VIRT10457|Blast_submission sp|P55118|LKA11_PASHA ASLTTISTALGAVSAGVSAAVGSAVGAPIALLVAGVTGLISGILEASKQAM RSVTAINTALAAIAGGVSAAGRGSVIASPIALLVSGITGVISTILQYSQAM *.*:*.****.**:*****. **.:.*****:****:***:***:***:*****

unk|VIRT10457|Blast_submission sp|P55118|LKA11_PASHA QGKILEWEKQNGGQNYFDKGYDSRYAAYLANNLKFLSELNKELEAERVIAIT HNKIVEWEKNNHGKNYFENGYDARYLANLQDNMKFLNLNKELEAERVIAIT :*.*:*****: * :****:****:****:****:****:****:****:*****

unk|VIRT10457|Blast_submission sp|P55118|LKA11_PASHA GELAGITKLGERIKSGKAYADAFEDGKKVEAGSNITLDAKTGIIDISNSNGK GDLAGISRLGEVKLSGKAYVDAFEEGKHLKADKLVQLDSANGIIDVSNSNGKA *:****:****: :****.****:****:****:****:****:****:****.

unk|VIRT10457|Blast_submission sp|P55118|LKA11_PASHA SPLLTAGTESRERLTNGKYSYINKLKFGGRVKNWQVTDGEASSKLDIFSKVIQ TPLLTPGTDERRVQTGKYEYITKLNINRVDSWKITDGAASSTFDLTNVVQR :****.**:****: .***.**.**:****:****:****:****:****:****

unk|VIRT10457|Blast_submission sp|P55118|LKA11_PASHA -ETEGTDEIGLIVNAKAGNDDIFVGQGKMNIDGGDGHDRVFSKDGGFGNIT GNVTKTKETKIVAKLGAGDDNVFGSGTTIEDGEGYDRVHYSR-GNYGALT .. *.* :***: *.*:****:****:****:****:****:****:****:****

unk|VIRT10457|Blast_submission sp|P55118|LKA11_PASHA AGSYTVNRKVARGDIYHEVVKRQETKVGKRTETIQRDYELRKVGYGYQSTD QGSYTVNRFVETGKALHEGTSTHTALVGNREEKIEYR-HSNNQHHAGYYTKD ***** * . ** .. : : *.*:****:****:****:****:****:****:****

unk|VIRT10457|Blast_submission sp|P55118|LKA11_PASHA IGSQFNDVFKGSKFNDIFHSGEbddLLDGGAGDDRLFGGKGNDRLSGDEGDD IGTSHNDIFKGSKFNDAFNGGDGVDTIDGKDGNDRLLFGGKGDDIDGGNGDD *.*:****:****:****:****:****:****:****:****:****:****:****

unk|VIRT10457|Blast_submission sp|P55118|LKA11_PASHA DVLNGGAGNDVYIFRKGDGNDTLYDGTGNDKLAFADANISDIMIERTKEII DLLHGGKGDDIFVHRQDGNDIITDSGDNDKLSFSDSNLKDLTFEKVKNLIV *.*:****:****:****:****:****:****:****:****:****:****:****

unk|VIRT10457|Blast_submission sp|P55118|LKA11_PASHA SINIPRWY---ITSNLQNYQSNKTDHKIEQLIGKDGSYITSQIDKILQDK KVTIQDWFWREADFAKEVRNYKATK-DEKIEEIIGQNGERITSKQVDDLI--A

unk|VIRT10457|Blast_submission .:. * *: ::::::**::.* *.****::**::*. ***.*::*:::
sp|P55118|LKA11_PASHA QELKKLADENKSQKLSASDIASSLNKLVGSMALFGTANSVSSNALQPITOPT
DELSKVVDNYELLKHS-KNVTNSLDKLISSASAFTSSNDSRNVLVAPTSMLD
:***.*:.*: : * * .:::.**::**::.* : * :*. . : * :

unk|VIRT10457|Blast_submission ----
sp|P55118|LKA11_PASHA ARAA